UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/803,687	03/09/2001	David T. Scadden	0492479-0018	7008

24280 7590 11/17/2005

CHOATE, HALL & STEWART LLP
TWO INTERNATIONAL PLACE
BOSTON, MA 02110

EXAMINER	
KATCHEVES, KONSTANTINA T	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/803,687	SCADDEN ET AL.	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 7/5/06

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-32,36,37,42-45 and 75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 7-32, 36, 37and 42-45 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 7-37and 42-45 and 75 are pending in the present application.

Response to Amendment

The rejection of claims 1, 3, 4, 7-11, 13, 15-18, 20, 22-29, 30, 36, 37, 43-45 and 75 under 35 U.S.C. 102(b) as being anticipated by Roberts et al. has been withdrawn for the reasons set forth in Applicant's remarks.

The rejection of claims 1-3, 7-37 and 42-45 and 75 under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. further in view of Waldman et al. are withdrawn from consideration for the reasons set forth in Applicant's remarks.

The rejection of claims 27 and 75 under 35 U.S.C. 112, first paragraph is withdrawn for the reasons set forth in Applicant's remarks.

New Grounds of Rejection

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 30-32 and 36-37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The instant claims are broadly drawn to stem or progenitor cells which may include an organism and as such are not appropriate subject matter under 35 U.S.C. 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-29, 42-45 and 75 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Nature of the invention and breadth of the claims

The nature of the invention involves therapeutic stem cell compositions and methods involving stem cells. The invention of the instant claims is broadly drawn to a method of expanding a stem or progenitor cell population and pharmaceutical composition comprising a therapeutically effective amount of stem or progenitor cells. Furthermore, the stem cells of the claimed method and composition embrace any type of stem and progenitor cell from any species including embryonic, adult, hematopoietic, neuronal, for example.

State of the prior art and unpredictability of the art

Although much promise is anticipated with stem cell methods and compositions, those of skill in the art have not yet realized that promise. The general challenges of stem cell expansion are recognized. Zhu et al. state that "sources of stem cells, large scale expansion, control of differentiations. . . represent formidable challenges." See Zhu et al. Current Drug Targets (2005 Feb.) 6(1) 97-110, abstract only. Some of the problems with stem cell expansion and growth involve chromosomal stability of the stem cells during prolonged growth in vivo. See Stojkovic et al. Reproduction (2004 Sep) 128(93) 259-67, page 260 (teaching that chromosomal aberrations are seen in human embryonic stem cells after prolonged growth). These two references show that the expansion of stem cells presents known challenges. Moreover, Stojkovic et al. also disclose that a further difficulty in expanding stem cell populations for therapeutic purposes is that culture of human embryonic stem cells requires the presence of feeder layers for the culture. The presence of feeder layers is not favorable for the derivation and

growth of clinical-grade human embryonic stem cell lines for therapeutic compositions. See Stojkovic et al. page 261.

Cheng (Oncogene (2004) 7256-7266) discusses at length many of the challenges of stem and progenitor cell growth and expansion. Cheng states: "Nevertheless, the functional difference in proliferative response between stem cells and progenitors represents a challenge for the specific manipulations of the stem cells for therapeutic purposes." The instant claims recite the same method for the proliferation and expansion of both stem and progenitor cells. Cheng states that the each of these two cell types responds differently to manipulations. Therefore it is unpredictable in the art to use the same methodology for cells known to respond differently to manipulations. Based on this unpredictability between hematopoietic stem cells and hematopoietic progenitor cells, which are related to each other, the question is raised whether the method claimed would work on any type of stem or progenitor cell from any source as claimed. See Cheng page 7257.

An additional observation from Cheng is specific to the role of p21 in the proliferation of stem and progenitor cells which is claimed as being "less than wild-type" in the present method. Cheng discloses that p21 -/- mice showed increased proliferation of hematopoietic stem cells. See Cheng page 7259. However, Cheng also discloses that "the role of p21 has been noted to positively affect proliferation after cytokine stimulation in progenitor cell pools." Therefore, it is unclear how the method would expand the populations of either stem or progenitor cells where p21 levels are less than wild type when in stem cells decreased levels promote proliferation while the presence, not absence, of p21 in progenitor cells promotes proliferation. See Cheng page 7259.

The specification also lacks enablement for therapeutically effective amounts of cells. Applicant fails to be enabled for the treatment of disease of any type by the present specification. Cheng acknowledges at some future time stem cells may be useful for therapeutic purposes, but much work remains. Cheng states that in addition to an understanding of cell cycle control, balancing self-renewing divisions of stem cells should be balanced with cell death or differentiation. See Cheng page 7264. Additionally, the problem of differentiation of stem cells grown in culture would also be a problem for making a pharmaceutical composition. As discussed by Stojkovic et al. cited above stem cell expansion and growth involve chromosomal instability of the stem which makes them suboptimal and unpredictable for pharmaceutical purposes. Czyz et al. (Biol. Chem., Vol. 384, pp 1391-1409 2003) clearly asserts the uncertainty relative to stem and progenitor cell therapies faced by those of skill in the art: "in the face of conflicting evidence, the true nature and therapeutic potential of such transdifferentiation phenomena remain uncertain. See Czyz et al. page 1391.

Guidance provide and presence of working examples in the specification

Applicant's specification fails to provide guidance and sufficient working examples to enable one of skill in the art to make and use the invention claimed. The specifications discussion is limited to hematopoietic stem cells and hematopoietic progenitor cells, yet the claims are drawn to any stem and progenitor cells from any source. Even given the disclosure discussing hematopoietic stem cells and hematopoietic progenitor cells, the art cited above raises questions as to the predictability of the art even as it relates to the cells disclosed in the specification. In consideration of each of the factors discussed above including the scope and

nature of the claims, the predictability and state of the art and the teachings of the specification, one of skill in the art is not enabled to make and use the invention as required by 35 U.S.C. 112, first paragraph.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (571) 272-0768. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 7:30 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Konstantina Katcheves
Examiner
Art Unit 1636

JAMES KETTER
PRIMARY EXAMINER